## d his

L15

(FILE 'HOME' ENTERED AT 15:23:28 ON 13 AUG 2007)

FILE 'BIOSIS, CAPLUS, EMBASE, MEDLINE, JAPIO' ENTERED AT 15:23:46 ON 13 AUG 2007 L1 1924 S (ANTI CD4 ANTIBOD?) L2 839 S (ANTI CD40 ANTIBOD?) 3 S L1 AND L2 L3L43 DUPLICATE REMOVE L3 (0 DUPLICATES REMOVED) L5 0 S (CDLOCD40HI) L6 6661 S CD4 AND CD40 L7 2554 S L6 AND ANTIBOD? 1638 S L7 AND PD<2004 L8 L9 876 DUPLICATE REMOVE L8 (762 DUPLICATES REMOVED) L10 34 S L9 AND DIABETES? 1 S L9 AND EMPHYSEMA? L11 L12 803 DUPLICATE REMOVE L1 (1121 DUPLICATES REMOVED) L13 661 S L12 AND PD<2004 7 S L9 AND L1 25 S L9 AND L2 L14

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L15 ANSWER 11 OF 25 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on
     STN
AN
     2000:432374 BIOSIS
DN
     PREV200000432374
TI
     Increased expression of CD40 ligand in activated CD4+
     T lymphocytes of systemic sclerosis patients.
ΑU
     Valentini, Gabriele [Reprint author]; Romano, Maria Fiammetta; Naclerio,
     Caterina; Bisogni, Rita; Lamberti, Annalisa; Turco, Maria Caterina;
     Venuta, Salvatore
     Istituto di Clinica Medica e Reumatologia, II Universita di Napoli, Via
CS
     Pansini, 5, 80131, Napoli, Italy
     Journal of Autoimmunity, (August, 2000) Vol. 15, No. 1, pp.
SO
     61-66. print.
     ISSN: 0896-8411.
DT .
     Article
     English
LA
ED
     Entered STN: 11 Oct 2000
     Last Updated on STN: 10 Jan 2002
AΒ
     CD40-CD154 interactions play a key role in regulating immune
     response and are involved in the development of some autoimmune diseases.
     We analysed the expression of CD154 antigen in CD3-activated PBMC from 10
     systemic sclerosis (SSc) patients and 10 control subjects by
     immunofluorescence. PBMC from SSc patients showed an increased expression
     of this molecule, since, 6 h following CD3 stimulation, the percentage of
     CD154+ cells was of 17.53+-2.0 (mean+-SE) in control and 25.33+-2.93 in
     patient cells (P<0.03). The higher expression of CD154 antigen was
     ascribible to CD4+ cells. The enhanced induction of CD154
     following CD3 stimulation depended on protein synthesis, since was
     abolished when the cells were stimulated via CD3 in the presence of
     cycloheximide. By analysing the expression of the CD40-induced
     antigen CD80, we verified that a blocking anti-CD40
     antibody inhibited CD80 appearance in SSc activated monocytes,
     indicating that CD154 molecule was functional. These results show an
     enhanced expression of a functional CD154 molecule in SSc CD4+
     activated T lymphocytes.
CC
     Cytology - Human
                        02508
     Cytology - Animal
                         02506
     Biochemistry studies - General
                                      10060
     Biochemistry studies - Proteins, peptides and amino acids
     Blood - Blood and lymph studies
                                      15002
     Blood - Blood cell studies
     Bones, joints, fasciae, connective and adipose tissue - Pathology
     Immunology - General and methods
                                        34502
     Immunology - Immunopathology, tissue immunology
IT
     Major Concepts
        Biochemistry and Molecular Biophysics; Clinical Immunology (Human
        Medicine, Medical Sciences)
ΙT
     Parts, Structures, & Systems of Organisms
        CD154-positive cells: blood and lymphatics, immune system; CD4
        -positive T lymphocytes: blood and lymphatics, immune system; PBMC:
        blood and lymphatics, immune system, CD3-activated
IT
     Diseases
        systemic sclerosis: connective tissue disease
        Sclerosis (MeSH)
ΙT
     Chemicals & Biochemicals
        CD154: expression, functionality; CD3; CD80: CD40-induced
        antigen, expression; anti-CD40 antibody;
        cycloheximide: protein synthesis inhibitor; protein: synthesis
ORGN Classifier
        Hominidae
                    86215
     Super Taxa
        Primates; Mammalia; Vertebrata; Chordata; Animalia
```

Organism Name

human: patient
Taxa Notes
Animals, Chordates, Humans, Mammals, Primates, Vertebrates
RN 66-81-9 (cycloheximide)

ANSWER 1 OF 7 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN ΑN 1995:438519 BIOSIS PREV199598452819 DN · Characteristics of antigen-independent and antigen-dependent interaction TТ of dendritic cells with CD4+ T cells. ΑU Hauss, Pascale; Selz, Francoise; Cavazzana-Calvo, Marina; Fischer, Alain [Reprint author] CS INSERM U429, Hop. Necker-Enfants Malades, 149 rue de Sevres, F-75743 Paris Cedex 15, France SO European Journal of Immunology, (1995) Vol. 25, No. 8, pp. 2285-2294. CODEN: EJIMAF. ISSN: 0014-2980. ·DT Article LA English ED Entered STN: 10 Oct 1995 Last Updated on STN: 10 Oct 1995 AΒ Dendritic cells (DC) are the main antigen-presenting cells for the initiation of primary T cell-mediated immune responses. In the first stage of activation, T cells bind to DC in an antigen-independent manner. We studied the adhesion characteristics of human CD4+ T cells to DC generated from CD34+ hematopoietic progenitors following 12 to 13 days of culture in the presence of granulocyte/macrophage colony-stimulating factor and tumor necrosis factor-alpha. A majority of these cells had the morphology, phenotype and functions of DC. CD4+ T/DC adhesion was measured by means of fluorescence microscopy and flow cytometry. independent receptor/ligand pathways, LFA-1/ICAM, ICAM/LFA-1, CD2/LFA-3 and CD28/CD80, were involved in the transient adhesion of DC to CD4+ T cells in antigen-independent and specific alloantigen-dependent situations, as shown by blocking experiments using monoclonal antibodies. The antibodies also blocked a primary mixed lymphocyte reaction (MLR) in which DC were used as stimulatory cells. Adhesion of alloreactive CD4+ T cells to antigen-presenting DC was stronger than that of resting CD4+  $\mathtt{T}$ cells, while peak adhesion occurred after 5 and 20 min, respectively. LFA-1 ligands involved in adhesion of resting CD4 T cells to DC and alloreactive CD4+ T-cells to specific DC differed in part, since ICAM-3 on resting T cells and ICAM-1 on alloreactive T lymphocytes preferentially bound LFA-1. Studies of interactions between DC and phorbol ester-activated T cells expressing the CD40 ligand revealed a fifth independent adhesion pathway, CD40/CD40 ligand. CD4-mediated regulation of CD4+ T/DC adhesion was suggested by the observation that preincubation of CD4+ T cells and DC individually with anti-CD4 antibodies inhibited adhesion. In addition, antibodies specific for HLA class II molecules inhibited adhesion when used to pretreat DC but not alloactivated CD4+ T cells. CC Cytology - Human 02508 Genetics - Human 03508 Biochemistry methods - Proteins, peptides and amino acids 10054 Biochemistry methods - Carbohydrates 10058 Biochemistry studies - Proteins, peptides and amino acids Biochemistry studies - Carbohydrates 10068 Biophysics - Methods and techniques · 10504 Biophysics - Molecular properties and macromolecules 10506 Biophysics - Membrane phenomena 10508 Blood - Blood cell studies 15004 Blood - Lymphatic tissue and reticuloendothelial system Bones, joints, fasciae, connective and adipose tissue - Anatomy 18002 Integumentary system - Anatomy 18502 Development and Embryology - Morphogenesis In vitro cellular and subcellular studies

Major Concepts
Biochemistry and Molecular Biophysics; Blood and Lymphatics (Transport

Immunology - Immunopathology, tissue immunology

ΙT

ANSWER 1 OF 7 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN 1995:438519 BIOSIS ΑN DN PREV199598452819 ΤI Characteristics of antigen-independent and antigen-dependent interaction of dendritic cells with CD4+ T cells. ΑU Hauss, Pascale; Selz, Francoise; Cavazzana-Calvo, Marina; Fischer, Alain [Reprint author] CS INSERM U429, Hop. Necker-Enfants Malades, 149 rue de Sevres, F-75743 Paris Cedex 15, France SO European Journal of Immunology, (1995) Vol. 25, No. 8, pp. 2285-2294. CODEN: EJIMAF. ISSN: 0014-2980. DT Article LA English ΕD Entered STN: 10 Oct 1995 Last Updated on STN: 10 Oct 1995 AΒ Dendritic cells (DC) are the main antigen-presenting cells for the initiation of primary T cell-mediated immune responses. In the first stage of activation, T cells bind to DC in an antigen-independent manner. We studied the adhesion characteristics of human CD4+ T cells to DC generated from CD34+ hematopoietic progenitors following 12 to 13 days of culture in the presence of granulocyte/macrophage colony-stimulating factor and tumor necrosis factor-alpha. A majority of these cells had the morphology, phenotype and functions of DC. CD4+ T/DC adhesion was measured by means of fluorescence microscopy and flow cytometry. Four independent receptor/ligand pathways, LFA-1/ICAM, ICAM/LFA-1, CD2/LFA-3 and CD28/CD80, were involved in the transient adhesion of DC to CD4+ T cells in antigen-independent and specific alloantigen-dependent situations, as shown by blocking experiments using monoclonal antibodies. The antibodies also blocked a primary mixed lymphocyte reaction (MLR) in which DC were used as stimulatory cells. Adhesion of alloreactive CD4+ T cells to antigen-presenting DC was stronger than that of resting CD4+ T cells, while peak adhesion occurred after 5 and 20 min, respectively. LFA-1 ligands involved in adhesion of resting CD4 T cells to DC and alloreactive CD4+ T-cells to specific DC differed in part, since ICAM-3 on resting T cells and ICAM-1 on alloreactive T lymphocytes preferentially bound LFA-1. Studies of interactions between DC and phorbol ester-activated T cells expressing the CD40 ligand revealed a fifth independent adhesion pathway, CD40/CD40 ligand. CD4-mediated regulation of CD4+ T/DC adhesion was suggested by the observation that preincubation of CD4+ T cells and DC individually with anti-CD4 antibodies inhibited adhesion. In addition, antibodies specific for HLA class II molecules inhibited adhesion when used to pretreat DC but not alloactivated CD4+ T cells. Cytology - Human CC 02508 Genetics - Human 03508 Biochemistry methods - Proteins, peptides and amino acids 10054 Biochemistry methods - Carbohydrates 10058 Biochemistry studies - Proteins, peptides and amino acids 10064 Biochemistry studies - Carbohydrates 10068 Biophysics - Methods and techniques 10504 Biophysics - Molecular properties and macromolecules 10506 Biophysics - Membrane phenomena 10508 Blood - Blood cell studies 15004 Blood - Lymphatic tissue and reticuloendothelial system Bones, joints, fasciae, connective and adipose tissue - Anatomy 18002

IT Major Concepts
Biochemistry and Molecular Biophysics; Blood and Lymphatics (Transport

18502

34508

Integumentary system - Anatomy

Development and Embryology - Morphogenesis In vitro cellular and subcellular studies

Immunology - Immunopathology, tissue immunology

and Circulation); Cell Biology; Clinical Endocrinology (Human Medicine, Medical Sciences); Development; Genetics; Integumentary System (Chemical Coordination and Homeostasis); Membranes (Cell Biology); Skeletal System (Movement and Support)

IT Miscellaneous Descriptors

ADHESION MOLECULES; ANTIGEN-PRESENTING CELL; T-HELPER CELL

ORGN Classifier

Hominidae 86215

Super Taxa

Primates; Mammalia; Vertebrata; Chordata; Animalia

Organism Name

human

Taxa Notes

Animals, Chordates, Humans, Mammals, Primates, Vertebrates

and Circulation); Cell Biology; Clinical Endocrinology (Human Medicine, Medical Sciences); Development; Genetics; Integumentary System (Chemical Coordination and Homeostasis); Membranes (Cell Biology); Skeletal System (Movement and Support)

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ADHESION MOLECULES; ANTIGEN-PRESENTING CELL; T-HELPER CELL

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Hominidae 86215

Super Taxa

Primates; Mammalia; Vertebrata; Chordata; Animalia

Organism Name

human

Taxa Notes

Animals, Chordates, Humans, Mammals, Primates, Vertebrates

ANSWER 24 OF 25 CAPLUS COPYRIGHT 2007 ACS on STN ΑN 1996:54899 CAPLUS DN 124:114965 Entered STN: 26 Jan 1996 EDB cell-B cell interaction through intercellular adhesion molecule-1 and TΙ lymphocyte functional antigen-1 regulates immunoglobulin E synthesis by B cells stimulated with interleukin-4 and anti-CD40 antibody ΑU Katada, Yoshinori; Tanaka, Toshio; Ochi, Hiroshi; Aitani, Masakazu; Yokota, Akira; Kikutani, Hitoshi; Suemura, Masaki; Kishimoto, Tadamitsu Department Medicine III, Osaka University Medical School, Osaka, Japan CS European Journal of Immunology (1996), 26(1), 192-200 SO CODEN: EJIMAF; ISSN: 0014-2980 PB VCH DT Journal LA English 15-3 (Immunochemistry) CC -IgE synthesis by purified human B cells is induced by two signals: a class switching factor, most commonly interleukin (IL)-4, and the engagement of CD40, which is activated through its interaction with CD40 ligand (CD40L) expressed on activated T cells. Thus, the combination of IL-4 and anti-CD40 monoclonal antibody (mAb) has been shown to stimulate IgE production in vitro by highly purified B cells. In this T cell-independent system, strong homotypic aggregation of B cells is observed prior to the production of IgE. Flow cytometric anal. and cell binding assays showed that the stimulation of purified B cells with anti-CD40 mAb plus IL-4 resulted in a striking increase of intercellular adhesion mol. (ICAM)-1(CD54) expression, an induction of CD43 and an avidity change of lymphocyte functional antigen (LFA)-1(CD11a/CD18), with little augmentation of CD18 expression. Addition of anti-ICAM-1 mAb caused an inhibition of homotypic aggregation but augmented IgE synthesis by B cells stimulated with anti-CD40 mAb and IL-4, although it did not affect B cell proliferation or IL-6 production by the B cells. Among the mAb against counter-receptors for ICAM-1 tested, anti-CD11a mAb suppressed IgE synthesis, while anti-CD18 mAb and anti-CD43 mAb had little effect. The enhancing or inhibitory effect of anti-ICAM-1 mAb or anti-CD11a mAb on IgE production was achieved by the increased or decreased expression of germline Co transcripts by B cells stimulated with anti-CD4 mAb and IL-4. These results indicate that B cell-B cell interaction through ICAM-1 and one of its counter receptors, LFA-1, regulates IgE synthesis by modulating Ca germ-line transcription. ST B cell IgE formation interleukin CD40; ICAM 1 LFA 1 IgE formation IT Transcription, genetic (B cell interaction through ICAM-1 and LFA-1 regulates IgE synthesis stimulated with interleukin-4 and anti-CD40 antibody) ΙT Lymphocyte (B-cell, B cell interaction through ICAM-1 and LFA-1 regulates IgE synthesis stimulated with interleukin-4 and anti-CD40 antibody) ΙT Antigens RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study) (CD40, B cell interaction through ICAM-1 and LFA-1 regulates IgE synthesis stimulated with interleukin-4 and anti-CD40 antibody) IT. Immunoglobulins RL: BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative) (E, B cell interaction through ICAM-1 and LFA-1 regulates IgE synthesis stimulated with interleukin-4 and anti-CD40

ANSWER 24 OF 25 CAPLUS COPYRIGHT 2007 ACS on STN ΑN 1996:54899 CAPLUS DN 124:114965 ED Entered STN: 26 Jan 1996 B cell-B cell interaction through intercellular adhesion molecule-1 and TΙ lymphocyte functional antigen-1 regulates immunoglobulin E synthesis by B cells stimulated with interleukin-4 and anti-CD40 antibody Katada, Yoshinori; Tanaka, Toshio; Ochi, Hiroshi; Aitani, Masakazu; Yokota, Akira; Kikutani, Hitoshi; Suemura, Masaki; Kishimoto, Tadamitsu Department Medicine III, Osaka University Medical School, Osaka, Japan ΑU CS European Journal of Immunology (1996), 26(1), 192-200 SO CODEN: EJIMAF; ISSN: 0014-2980 PB VCH DT Journal English LA CC 15-3 (Immunochemistry) AΒ IgE synthesis by purified human B cells is induced by two signals: a class switching factor, most commonly interleukin (IL)-4, and the engagement of CD40, which is activated through its interaction with CD40 ligand (CD40L) expressed on activated T cells. Thus, the combination of IL-4 and anti-CD40 monoclonal antibody (mAb) has been shown to stimulate IgE production in vitro by highly purified B cells. In this T cell-independent system, strong homotypic aggregation of B cells is observed prior to the production of IgE. Flow cytometric anal. and cell binding assays showed that the stimulation of purified B cells with anti-CD40 mAb plus IL-4 resulted in a striking increase of intercellular adhesion mol. (ICAM)-1(CD54) expression, an induction of CD43 and an avidity change of lymphocyte functional antigen (LFA)-1(CD11a/CD18), with little augmentation of CD18 expression. Addition of anti-ICAM-1 mAb caused an inhibition of homotypic aggregation but augmented IgE synthesis by B cells stimulated with anti-CD40 mAb and IL-4, although it did not affect B cell proliferation or IL-6 production by the B cells. Among the mAb against counter-receptors for ICAM-1 tested, anti-CD11a mAb suppressed IgE synthesis, while anti-CD18 mAb and anti-CD43 mAb had little effect. The enhancing or inhibitory effect of anti-ICAM-1 mAb or anti-CD11a mAb on IgE production was achieved by the increased or decreased expression of germline Ca transcripts by B cells stimulated with anti-CD4 mAb and IL-4. These results indicate that B cell-B cell interaction through ICAM-1 and one of its counter receptors, LFA-1, regulates IgE synthesis by modulating Ca germ-line transcription. ST B cell IgE formation interleukin CD40; ICAM 1 LFA 1 IgE formation IT Transcription, genetic (B cell interaction through ICAM-1 and LFA-1 regulates IgE synthesis stimulated with interleukin-4 and anti-CD40 antibody) IT Lymphocyte (B-cell, B cell interaction through ICAM-1 and LFA-1 regulates IgE synthesis stimulated with interleukin-4 and anti-CD40 antibody) IT Antigens RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study) (CD40, B cell interaction through ICAM-1 and LFA-1 regulates IgE synthesis stimulated with interleukin-4 and anti-CD40 antibody) ITImmunoglobulins RL: BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative) (E, B cell interaction through ICAM-1 and LFA-1 regulates IgE synthesis

stimulated with interleukin-4 and anti-CD40

antibody)

IT Glycoproteins, specific or class
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)

(ICAM-1 (intercellular adhesion mol. 1), B cell interaction through ICAM-1 and LFA-1 regulates IgE synthesis stimulated with interleukin-4 and anti-CD40 antibody)

IT Integrins
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)

(antigens LFA-1, B cell interaction through ICAM-1 and LFA-1 regulates IgE synthesis stimulated with interleukin-4 and anti-

Sialoglycoproteins
RL: BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL
(Biological study); FORM (Formation, nonpreparative)
 (leukosialins, B cell interaction through ICAM-1 and LFA-1 regulates
 IgE synthesis stimulated with interleukin-4 and anti CD40 antibody)

antibody)

IT Glycoproteins, specific or class

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)

(ICAM-1 (intercellular adhesion mol. 1), B cell interaction through ICAM-1 and LFA-1 regulates IgE synthesis stimulated with interleukin-4 and anti-CD40 antibody)

IT Integrins

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)

(antigens LFA-1, B cell interaction through ICAM-1 and LFA-1 regulates IgE synthesis stimulated with interleukin-4 and anti-CD40 antibody)

IT Lymphokines and Cytokines

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)

(interleukin 4, B cell interaction through ICAM-1 and LFA-1 regulates IgE synthesis stimulated with interleukin-4 and anti-CD40 antibody)

IT Sialoglycoproteins

RL: BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative)

(leukosialins, B cell interaction through ICAM-1 and LFA-1 regulates IgE synthesis stimulated with interleukin-4 and anti-CD40 antibody)

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ANSWER 22 OF 25 CAPLUS COPYRIGHT 2007 ACS on STN
     1998:566926 CAPLUS
AN
DN
     129:314876
ED
     Entered STN: 07 Sep 1998
ΤI
     Surface expression and release of soluble forms of CD8 and CD23 in
     CD40- and IL-4-activated mononuclear cells from patients with .
     Graves' disease (GD)
· AU
     Itoh, M.; Uchimura, K.; Hayakawa, N.; Makino, M.; Hayashi, R.; Nagata, M.;
     Kakizawa, H.; Nagasaka, A.; Sakamoto, H.; Kuzuya, H.
     Department of Internal Medicine, School of Medicine, Fujita Health
     University, Aichi, 470-1192, Japan
SO
     Clinical and Experimental Immunology (1998), 113(2), 309-314
     CODEN: CEXIAL; ISSN: 0009-9104
PB
     Blackwell Science Ltd.
DT
     Journal
LA
     English
CC
     15-8 (Immunochemistry)
     The authors investigated the effect of T cell-dependent B cell activation
     on the surface expression and release of the soluble forms of CD8 and CD23 by
     peripheral blood mononuclear cells (PBMC) obtained from patients with GD
     vs. patients with Hashimoto's thyroiditis, and normal controls.
     Incubating the PBMC with anti-CD40 MoAbs and IL-4 increased the
     soluble CD23 levels in cells from all three groups. An increase in the number
     of CD23+ cells was observed in the PBMC from the patients with GD but not in
     PBMC from Hashimoto's thyroiditis or controls. Less soluble CD8 was released
     from anti-CD40 antibody and IL-4-stimulated
     PBMC obtained from patients with GD relative to those from the controls.
     In addition, the number of CD8+ cells was significantly reduced in stimulated
     PBMC from the GD patients relative to those from controls. Incubation of
     PBMC with anti-CD40 antibody plus IL-4 did
     not affect the proportions of CD4+, CD20+, Fas+CD4+,
     and Fas+CD8+ cells. The addition of T3 to cultured PBMC from controls did
     not reproduce the changes in CD23+ and CD8+ cells noted in the samples
     from GD patients. Thus, T cell-dependent B cell activation, mediated by a
     CD40 pathway, may reduce the number of CD8+ cells, causing
     exacerbation of GD.
ST
     CD8 CD40 interleukin 4 Graves disease; CD23 CD40
     interleukin 4 Graves disease
TT
     Cell activation
        (B cell; soluble CD8 and CD23 expression in CD40- and
        IL-4-activated mononuclear cells from humans with Graves' disease)
ΙT
     Immunoglobulin receptors
     RL: BOC (Biological occurrence); BSU (Biological study, unclassified);
     BIOL (Biological study); OCCU (Occurrence)
        (IgE type II, soluble; soluble CD8 and CD23 expression in CD40- and
        IL-4-activated mononuclear cells from humans with Graves' disease)
TI
     B cell (lymphocyte)
        (activation; soluble CD8 and CD23 expression in CD40- and
        'IL-4-activated mononuclear cells from humans with Graves' disease)
ΙT
     Graves' disease
     T cell (lymphocyte)
        (soluble CD8 and CD23 expression in CD40- and IL-4-activated
        mononuclear cells from humans with Graves' disease)
ΙT
     CD40 (antigen)
     Interleukin 4
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); BIOL (Biological study)
        (soluble CD8 and CD23 expression in CD40- and IL-4-activated
        mononuclear cells from humans with Graves' disease)
ΙT
     CD8 (antigen)
     RL: BOC (Biological occurrence); BSU (Biological study, unclassified);
     BIOL (Biological study); OCCU (Occurrence)
        (soluble; soluble CD8 and CD23 expression in CD40- and
        IL-4-activated mononuclear cells from humans with Graves' disease)
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ANSWER 22 OF 25 CAPLUS COPYRIGHT 2007 ACS on STN
     1998:566926 CAPLUS
ΑN
DN
     129:314876
ΕD
     Entered STN: 07 Sep 1998
TI
     Surface expression and release of soluble forms of CD8 and CD23 in
     CD40- and IL-4-activated mononuclear cells from patients with
     Graves' disease (GD)
     Itoh, M.; Uchimura, K.; Hayakawa, N.; Makino, M.; Hayashi, R.; Nagata, M.;
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     Kakizawa, H.; Nagasaka, A.; Sakamoto, H.; Kuzuya, H.
     Department of Internal Medicine, School of Medicine, Fujita Health
     University, Aichi, 470-1192, Japan
SO
     Clinical and Experimental Immunology (1998), 113(2), 309-314
     CODEN: CEXIAL; ISSN: 0009-9104
PB
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ST
     CD8 CD40 interleukin 4 Graves disease; CD23 CD40
     interleukin 4 Graves disease
ΙT
     Cell activation
        (B cell; soluble CD8 and CD23 expression in CD40- and
        IL-4-activated mononuclear cells from humans with Graves' disease)
     Immunoglobulin receptors
IΤ
     RL: BOC (Biological occurrence); BSU (Biological study, unclassified);
     BIOL (Biological study); OCCU (Occurrence)
        (IgE type II, soluble; soluble CD8 and CD23 expression in CD40- and
        IL-4-activated mononuclear cells from humans with Graves' disease)
IT .
     B cell (lymphocyte)
        (activation; soluble CD8 and CD23 expression in CD40- and
        IL-4-activated mononuclear cells from humans with Graves' disease)
IT
     Graves' disease
     T cell (lymphocyte)
        (soluble CD8 and CD23 expression in CD40- and IL-4-activated
        mononuclear cells from humans with Graves' disease)
IT
     CD40 (antigen)
     Interleukin 4
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); BIOL (Biological study)
        (soluble CD8 and CD23 expression in CD40- and IL-4-activated
        mononuclear cells from humans with Graves' disease)
IT
     CD8 (antigen)
     RL: BOC (Biological occurrence); BSU (Biological study, unclassified);
     BIOL (Biological study); OCCU (Occurrence)
        (soluble; soluble CD8 and CD23 expression in CD40- and
        IL-4-activated mononuclear cells from humans with Graves' disease)
```

38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD RE

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- (26) Raikow, R; Ophthalmology 1990, V97, P629 MEDLINE
- (27) Sayinalp, S; Horm Metab Res 1996, V28, P133 CAPLUS
- (28) Smith, B; Endocr Rev 1988, V9, P106 CAPLUS
- (29) Sridama, V; J Clin Endocrinol Metab 1982, V54, P316 MEDLINE
- (30) Swendeman, S; EMBO J 1987, V6, P1637 CAPLUS
- (31) Tomkinson, B; J Immunol 1989, V142, P2230 CAPLUS
- (32) Tsubata, T; Nature 1993, V364, P645 CAPLUS
- (33) Valentine, M; Eur J Immunol 1992, V22, P3141 CAPLUS
- (34) Valle, A; Eur J Immunol 1989, V19, P1463 CAPLUS
- (35) Walfish, P; Autoimmunity 1992, V13, P35 MEDLINE
- (36) Wall, J; J Clin Endocrinol Metab 1983, V56, P164 MEDLINE
- (37) Weetman, A; Endocr Rev 1984, V5, P309 MEDLINE
- (38) Werner, S; N Engl J Med 1972, V287, P421 MEDLINE

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ANSWER 14 OF 25
                  BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on
ΑN
     1994:178029 BIOSIS
DN
     PREV199497191029
ΤI
     Activated CD4+ T cells induce CD40-dependent
     proliferation of human B cell precursors.
ΑU
     Renard, Nathalie [Reprint author]; Duvert, Valerie; Blanchard, Dominique;
     Banchereau, Jacques; Saeland, Sem
CS
     Schering-Plough, Lab. Immunological Res., 27 chemin des Peupliers, 69571
     Dardilly, France
     Journal of Immunology, (1994) Vol. 152, No. 4, pp. 1693-1701.
SO
     CODEN: JOIMA3. ISSN: 0022-1767.
DT
     Article
LA
     English
ED
     Entered STN: 26 Apr 1994
     Last Updated on STN: 26 Apr 1994
AΒ
     Anti-CD3-activated human CD4+ T cell clones were found to induce.
     proliferation of CD10+, CD19+, surface(s) Ig-B cell precursors (BCP)
     isolated from human fetal bone marrow. The great majority of the B
     lineage cells recovered in cocultures of BCP and activated T cells
     displayed a BCP phenotype (Ig- or cytoplasmic mu+ and K/lambda-),
     including most of the cycling cells, indicating that the cultures do not
     favor a transition to mature B cells. Supernatants of activated T cells
     were ineffective in inducing BCP proliferation, indicating the necessity
     of close association with stimulator cells. In line with this finding,
     the CD40 molecule was found to represent an important component
     of the cocultures, as BCP proliferation was strongly inhibited by soluble
     anti-CD40 antibody. In addition, CD4
     + T cell clones from a hyper-IgM patient expressing a truncated
     CD40 ligand (CD40-L) failed to induce BCP proliferation.
     Finally, a combination of cytokines (IL-2, IL-3, IL-7, and IL-10) enhanced
     the observed T cell-dependent BCP proliferation, but could not substitute
     for the deficient CD40-L. Taken together, our data demonstrate
     that CD4+ T cells exert a stimulatory effect on in vitro B human
     lymphopoiesis via the CD40 pathway. The present results suggest
     that T cells may play an important role in regulating B cell ontogeny in
     the bone marrow.
CC
     Microscopy - Cytology and cytochemistry
                        02508
     Cytology - Human
     Genetics - Human
                        03508
     Radiation biology - Radiation and isotope techniques
     Biochemistry studies - Proteins, peptides and amino acids 10064
     Biochemistry studies - Carbohydrates
     Biophysics - Molecular properties and macromolecules
     Biophysics - Membrane phenomena
                                       10508
     Blood - Blood cell studies
                                  15004
     Blood - Lymphatic tissue and reticuloendothelial system
     Bones, joints, fasciae, connective and adipose tissue - General and
               18001
     Bones, joints, fasciae, connective and adipose tissue - Anatomy
     Development and Embryology - Morphogenesis
                                                  25508
     In vitro cellular and subcellular studies
     Immunology - General and methods
                                        34502
     Immunology - Immunopathology, tissue immunology
                                                       34508
ΙT
     Major Concepts
        Biochemistry and Molecular Biophysics; Blood and Lymphatics (Transport
        and Circulation); Cell Biology; Clinical Endocrinology (Human Medicine,
        Medical Sciences); Development; Genetics; Immune System (Chemical
        Coordination and Homeostasis); Membranes (Cell Biology); Skeletal
        System (Movement and Support)
     Miscellaneous Descriptors
        B-CELL ONTOGENY; B-LYMPHOPOIESIS; BONE MARROW; CYTOFLUOROMETRY
ORGN Classifier
```

Hominidae

86215

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ANSWER 14 OF 25 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on
     STN
AN
     1994:178029 BIOSIS
DN
     PREV199497191029
     Activated CD4+ T cells induce CD40-dependent
ΤI
     proliferation of human B cell precursors.
ΑU
     Renard, Nathalie [Reprint author]; Duvert, Valerie; Blanchard, Dominique;
     Banchereau, Jacques; Saeland, Sem
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     Schering-Plough, Lab. Immunological Res., 27 chemin des Peupliers, 69571
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     Journal of Immunology, (1994) Vol. 152, No. 4, pp. 1693-1701.
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DT
     Article
LA
     English
ED
     Entered STN: 26 Apr 1994
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     Anti-CD3-activated human CD4+ T cell clones were found to induce
AΒ
     proliferation of CD10+, CD19+, surface(s) Ig-B cell precursors (BCP)
     isolated from human fetal bone marrow. The great majority of the B
     lineage cells recovered in cocultures of BCP and activated T cells
    displayed a BCP phenotype (Ig- or cytoplasmic mu+ and K/lambda-),
    including most of the cycling cells, indicating that the cultures do not
     favor a transition to mature B cells. Supernatants of activated T cells
     were ineffective in inducing BCP proliferation, indicating the necessity
     of close association with stimulator cells. In line with this finding,
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     + T cell clones from a hyper-IgM patient expressing a truncated
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     Finally, a combination of cytokines (IL-2, IL-3, IL-7, and IL-10) enhanced
     the observed T cell-dependent BCP proliferation, but could not substitute
     for the deficient CD40-L. Taken together, our data demonstrate
     that CD4+ T cells exert a stimulatory effect on in vitro B human
     lymphopoiesis via the CD40 pathway. The present results suggest
     that T cells may play an important role in regulating B cell ontogeny in
     the bone marrow.
CC
     Microscopy - Cytology and cytochemistry 01054
                       02508
     Cytology - Human
     Genetics - Human
                        03508
     Radiation biology - Radiation and isotope techniques
     Biochemistry studies - Proteins, peptides and amino acids
     Biochemistry studies - Carbohydrates
                                            10068
     Biophysics - Molecular properties and macromolecules
     Biophysics - Membrane phenomena
                                       10508
     Blood - Blood cell studies
                                  15004
     Blood - Lymphatic tissue and reticuloendothelial system
     Bones, joints, fasciae, connective and adipose tissue - General and
               18001
     Bones, joints, fasciae, connective and adipose tissue - Anatomy
     Development and Embryology - Morphogenesis 25508
     In vitro cellular and subcellular studies
                                                 32600
     Immunology - General and methods
                                       34502
     Immunology - Immunopathology, tissue immunology
                                                       34508
ΙT
     Major Concepts
        Biochemistry and Molecular Biophysics; Blood and Lymphatics (Transport
        and Circulation); Cell Biology; Clinical Endocrinology (Human Medicine,
        Medical Sciences); Development; Genetics; Immune System (Chemical
        Coordination and Homeostasis); Membranes (Cell Biology); Skeletal
        System (Movement and Support)
ΙT
     Miscellaneous Descriptors
        B-CELL ONTOGENY; B-LYMPHOPOIESIS; BONE MARROW; CYTOFLUOROMETRY
ORGN Classifier
        Hominidae
                    86215
```

Super Taxa
 Primates; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
 Hominidae
Taxa Notes
 Animals, Chordates, Humans, Mammals, Primates, Vertebrates

Super Taxa
Primates; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
Hominidaé
Taxa Notes
Animals, Chordates, Humans, Mammals, Primates, Vertebrates

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ANSWER 11 OF 25 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on
L15
AN
     2000:432374 BIOSIS
     PREV200000432374
DN
TI ·
     Increased expression of CD40 ligand in activated CD4+
     T lymphocytes of systemic sclerosis patients.
ΑU
     Valentini, Gabriele [Reprint author]; Romano, Maria Fiammetta; Naclerio,
     Caterina; Bisogni, Rita; Lamberti, Annalisa; Turco, Maria Caterina;
     Venuta, Salvatore
    Istituto di Clinica Medica e Reumatologia, II Universita di Napoli, Via
CS
     Pansini, 5, 80131, Napoli, Italy
     Journal of Autoimmunity, (August, 2000) Vol. 15, No. 1, pp.
SO
     61-66. print.
     ISSN: 0896-8411.
DT
     Article
LA
     English
     Entered STN: 11 Oct 2000
     Last Updated on STN: 10 Jan 2002
     CD40-CD154 interactions play a key role in regulating immune
     response and are involved in the development of some autoimmune diseases.
     We analysed the expression of CD154 antigen in CD3-activated PBMC from 10
     systemic sclerosis (SSc) patients and 10 control subjects by
     immunofluorescence. PBMC from SSc patients showed an increased expression
     of this molecule, since, 6 h following CD3 stimulation, the percentage of
     CD154+ cells was of 17.53+-2.0 (mean+-SE) in control and 25.33+-2.93 in
     patient cells (P<0.03). The higher expression of CD154 antigen was
     ascribible to CD4+ cells. The enhanced induction of CD154
     following CD3 stimulation depended on protein synthesis, since was
     abolished when the cells were stimulated via CD3 in the presence of
     cycloheximide. By analysing the expression of the CD40-induced
     antigen CD80, we verified that a blocking anti-CD40
     antibody inhibited CD80 appearance in SSc activated monocytes,
     indicating that CD154 molecule was functional. These results show an
     enhanced expression of a functional CD154 molecule in SSc CD4+
     activated T lymphocytes.
     Cytology - Human
                        02508
     Cytology - Animal
                         02506
     Biochemistry studies - General
                                      10060
     Biochemistry studies - Proteins, peptides and amino acids
     Blood - Blood and lymph studies
                                       15002
     Blood - Blood cell studies
     Bones, joints, fasciae, connective and adipose tissue - Pathology
                                                                          18006
     Immunology - General and methods
                                        34502
     Immunology - Immunopathology, tissue immunology
ΙT
     Major Concepts
        Biochemistry and Molecular Biophysics; Clinical Immunology (Human
        Medicine, Medical Sciences)
ΙT
     Parts, Structures, & Systems of Organisms
        CD154-positive cells: blood and lymphatics, immune system; CD4
        -positive T lymphocytes: blood and lymphatics, immune system; PBMC:
        blood and lymphatics, immune system, CD3-activated
ΙT
     Diseases
        systemic sclerosis: connective tissue disease
        Sclerosis (MeSH)
     Chemicals & Biochemicals
IT
        CD154: expression, functionality; CD3; CD80: CD40-induced
        antigen, expression; anti-CD40 antibody;
        cycloheximide: protein synthesis inhibitor; protein: synthesis
ORGN Classifier
        Hominidae
                    86215
     Super Taxa
        Primates; Mammalia; Vertebrata; Chordata; Animalia
```

Organism Name

human: patient
Taxa Notes
Animals, Chordates, Humans, Mammals, Primates, Vertebrates
RN 66-81-9 (cycloheximide)

## (FILE 'HOME' ENTERED AT 15:23:28 ON 13 AUG 2007)

FILE 'BIOSIS, CAPLUS, EMBASE, MEDLINE, JAPIO' ENTERED AT 15:23:46 ON 13 AUG 2007

	1100 201	0,	
L1		1924	S (ANTI CD4 ANTIBOD?)
L2		839	S (ANTI CD40 ANTIBOD?)
L3	•	3	S L1 AND L2
L4		3	DUPLICATE REMOVE L3 (0 DUPLICATES REMOVED)
L5		0	S (CDLOCD40HI)
L6	. (	6661	S CD4 AND CD40
L7	2	2554	S L6 AND ANTIBOD?
L8		1638	S L7 AND PD<2004
L9	•	876	DUPLICATE REMOVE L8 (762 DUPLICATES REMOVED)
L10		34	S L9 AND DIABETES?
L11		1	S L9 AND EMPHYSEMA?
L12		803	DUPLICATE REMOVE L1 (1121 DUPLICATES REMOVED)
L13		661	S L12 AND PD<2004
L14		7	S L9 AND L1
T.15		. 25	S 1.9 AND 1.2



WC001407

Day: Monday Date: 8/13/2007 Time: 11:36:10

## Biotech Query for 10/563570

Title: METHODS FOR PREDICTING DEVELOPMENT OF AUTO-IMMUNE DISEASES AND TREATMENT OF SAME

Inventor: WAGNER, DAVID

Location:

Location Date:

Group Art Unit: 1641

Status: 71/RESPONSE TO NON-FINAL OFFICE ACTION ENTERED AND FORWARDED TO

**EXAMINER** 

Barcode:

Filing or 371(c) Date: 08/25/2006

Num	Date	Code	Contents Description
4	01/26/2006	CRFE	CRF IS GOOD TECHNICALLY / ENTERED INTO DATABASE

Search for Biotech I	nfo: Application	on#	Search
	PCT /	[/   	earch;
	Bar Code #		Search

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